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Hematologic laboratory changes during post COVID 19 in children

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Abstract

The COVID-19 pandemic has affected millions globally, with a notable impact on pediatric patients. Hematologic and inflammatory changes in children with COVID-19 can provide key insights into disease severity, recovery patterns, and the likelihood of complications. This study investigates the role of specific hematologic markers in predicting clinical outcomes such as length of hospitalization and the presence of respiratory symptoms in pediatric patients' post-COVID-19. Descriptive analysis showed that 67.1% of patients presented with respiratory symptoms, while 47.1% had elevated neutrophil levels, 57.9% had low lymphocyte levels, and 55% had high CRP levels. Significant associations are identified between elevated neutrophil with longer hospitalization and respiratory complications, while lower lymphocyte and platelet levels were linked to shorter stays.

Keywords: Hematologic Markers; Neutrophilia; Lymphopenia; Post COVID 19; Severity; Pediatric Patient

1. Introduction

Since the early stages of the COVID-19 pandemic, when children typically made up only around 2% of laboratory-confirmed SARS-CoV-2 cases, the number of infected children has increased significantly. This is due to changes in the criteria for SARS-CoV-2 testing, as the risks of exposure, COVID-19-related symptoms, laboratory testing capacity, and priority populations have evolved throughout the pandemic. Children of all ages can become infected with COVID-19. The youngest diagnosed child was one day old, and the oldest was 17 years old. The average age of infection among children has been found to be 6–7 years. (1,2,6) Studies have reported that COVID-19 had a higher incidence in males than females. (1,5,7) Multiple reports have shown that children generally experienced a milder form of the disease compared to adults. (11) Several hypotheses or theories have been proposed to explain this, including:

1.1. Reduced thrombin and fibrin formation

Children may have a lower risk of acute respiratory distress syndrome (ARDS) associated with COVID-19 due to reduced generation of thrombin and fibrin. (3,4)

1.2. Angiotensin-converting enzyme 2 (ACE2) and the renin-angiotensin system

ACE2 is a regulatory enzyme in the renin-angiotensin system (RAS), which converts angiotensin-2 into angiotensin 1–7 After entering pneumocytes, SARS-CoV-2 downregulates ACE2 expression, lowering angiotensin-2 metabolism. Elevated angiotensin-2 levels have been found in COVID-19 patients compared to healthy adults. One proposed

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hypothesis is that the cellular expression of the ACE2 receptor and its interaction with the virus's spike (S) protein might differ between children and adults, potentially accounting for the milder disease in children. (13)

1.3. Lung development effects

Good regenerative capacity might explain the overall milder severity and early recovery from COVID-19 in children. Due to greater resistance in the upper airways, aerosol particles tend to deposit more in the tracheobronchial tree than in the alveoli in children. This could lead to more bronchiolitis-like infections and fewer cases of pneumonia caused by SARS-CoV-2. From a physiological standpoint, a higher frequency of ciliary movement in lung epithelial cells in children may hinder the virus's entry into pulmonary pneumocytes. (11,14,17)

1.4. Differences in the immune system between adults and children

The immune system changes with age in both physiology and function, especially through the process of immunosenescence, which refers to the gradual decline in immune function due to natural aging. Immunosenescence, driven by thymic involution, is associated with a gradual reduction in T cell count and activity. In children, increased thymic activity means greater T cell numbers and function, offering better protection against viral infections. Their immature and not fully developed immune system may explain why they don't develop a strong inflammatory response, thereby reducing host-mediated damage. (8,9,15)

1.4.1. Innate immunity in children

The lack of co-infections and comorbidities (such as diabetes, hypertension, and chronic lung or heart diseases), along with lower exposure to airborne particles and pollutants, helps protect children's lungs and respiratory tracts. (16,18)

Among the hematologic alterations related to post-COVID-19, the following have been identified:

1.4.2. Lymphopenia

This is associated with a decrease in CD4+ and CD8+ T lymphocytes, believed to occur via several mechanisms. SARS-CoV-2 enters human cells by binding to the ACE2 receptor, found primarily in the lungs, heart, and gastrointestinal tract. (2,3) These receptors are also expressed on lymphocyte surfaces. Therefore, SARS-CoV-2 may directly bind to these cells and cause their lysis. The infection also triggers the release of multiple inflammatory cytokines. This intense cytokine activation can promote lymphocyte apoptosis and lead to lymphoid organ atrophy, thereby reducing lymphocyte regeneration. Additionally, CD4+ T cells play a critical role in immune modulation, including the regulation of inflammatory responses. (3,4,5)

1.4.3. Neutrophilia

The immune dysregulation associated with COVID-19 leads to increased neutrophil production and lymphocyte apoptosis. Thus, neutrophilia corresponds with lymphopenia. It may also be secondary to superimposed bacterial infections, more likely in patients with severe illness. The hyperinflammatory response and cytokine surge stimulate exaggerated infiltration of neutrophils, macrophages, and monocytes into the pulmonary parenchyma, exacerbating COVID-19 infection. (16,20)

1.4.4. Thrombocytosis

The overall prevalence of thrombosis in children with COVID-19 is significantly lower than in adults. Thrombosis risk increases in patients with MIS-C, especially those with severe ventricular dysfunction or coronary artery aneurysms. Thromboembolic events during COVID-19 and MIS-C occur not only in venous areas (including deep vein thrombosis (DVT), central venous sinus thrombosis (CVST), pulmonary embolism (PE), and splanchnic vein thrombosis (SVT)) but also in cerebral arteries, causing acute ischemic stroke (AIS), and more rarely in coronary or peripheral arteries. Intracardiac thrombosis (ICT) has also been described. (7,8,10)

Aim

The aim of this study is to explore the relationship between hematologic markers, such as neutrophil, lymphocyte, platelets and their impact on clinical outcomes in pediatric patients recovering from COVID-19. This includes assessing their influence on hospital stay duration and respiratory complications.

2. Methodology

The study included a total of 140 pediatric patients confirmed with positive COVID-19 IgG and admitted to the General Pediatrics Ward, QSUT January 2021- December 2023. Data was collected from clinical documentation and laboratory examinations, focusing on hematologic parameters (neutrophil, lymphocyte, platelet levels) and the relationship between these markers and clinical outcomes.

3. Results

Of the 140 hospitalized children included in the study the largest age group consisted of infants (0–12 months), representing 31.4% of the total number of patients. Children aged 4–10 years made up 30.7% of the population, followed by children aged 10–14 years (19.3%) and toddlers aged 1–3 years (18.6%). The distribution shows that the majority of patients were either infants or children under the age of 10. Out of 140 patients, 60% (84 patients) were male and 40% (56 patients) were female. This indicates a higher prevalence of males in the study population.

Table 1 Distribution by age group

Age	Frequency	Percentage (%)
0-12 months	44	31,4
1 -3 years old	26	18,6
4-10 years old	43	30,7
10-14 years old	27	19,3

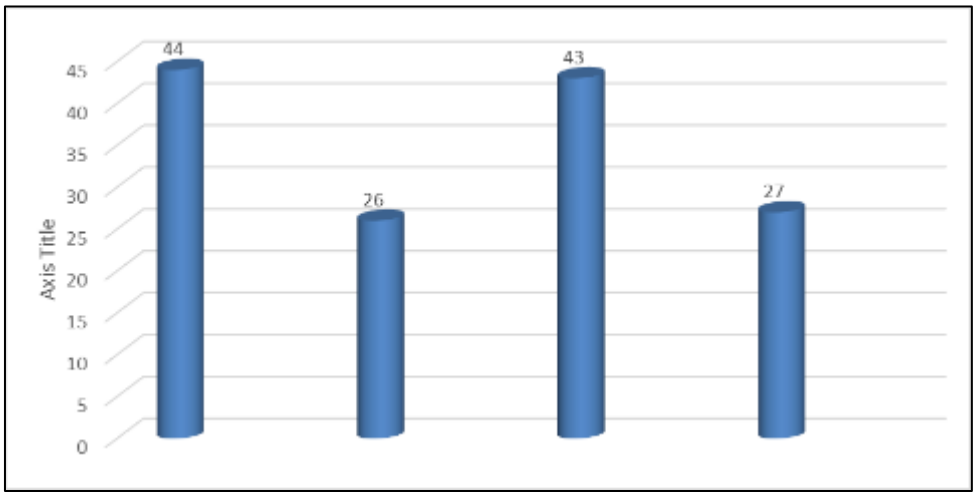

Figure 1 Haemoglobin degree (X axis haemoglobin degree, Y axis percentage of cases in children)

Furthermore, the presence of comorbidities and the duration of hospital stay were analyzed.

Table 2 Distribution According to the Presence of Comorbidities

Comorbidities	Frequency	Percentage (%)
Congenital Cardiovascular Diseases	5	3,6
Respiratory tract disorders	10	7,1
Type I Diabetes and Other Metabolic Disorders	8	5,7
Gastrointestinal tract disorders	7	5,0
Autism Spectrum Disorders and Intellectual Disability	6	4,3
Urinary tract disorders	4	2,8
Others	7	5,0
Without coomorbidities	93	66,4
Total	140	100%

Among the 140 pediatric patients, 7.1% had a history of recurrent respiratory infections or frequent hospitalizations, followed by patients with metabolic disorders, such as type 1 diabetes, in 5.7% of cases, and gastrointestinal disorders in 5% of them. Around 3.6% of these patients suffered from congenital cardiovascular diseases, 4.3% presented with neurodevelopmental disorders, including autism and intellectual delays, and 2.9% had genitourinary disorders. These findings highlight that respiratory and metabolic disorders are the most common comorbid conditions in this group. Clinical symptoms and the duration of symptoms prior to hospitalization were also analyzed

Table 3 Symptoms and duration of symptoms before hospitalization."

	Frequency	%
Respiratory symptoms	94	67,1
Gastrointestinal symptoms	26	18,6
Other symptoms	20	14,3

Complete blood count laboratory parameters were analyzed: leukocytes, platelets, neutrophils, lymphocytes, and hemoglobin. Based on reference values, and for research convenience, the results were classified as: below normal, within normal range, or above normal.

Table 4 Complete blood count laboratory parameters

Parameters	Above normal		Normal		Below normal	
	n	%	n	%	n	%
Hemoglobin	20	14,3	80	57,1	40	28,6
Leukocytes	30	21,4	85	60,7	25	17,9
Thrombocytes	6	4,3	59	42,1	75	53,6
Erithrocytes	15	10,7	90	64,3	35	25,0
Neutrophils	66	47,1	41	29,3	33	23,6
Lymphocytes	14	10,0	45	32,1	81	57,9
NLR	50	35,7	65	46,4	25	17,9

*NLR = Neutrophil-to-Lymphocyte Ratio

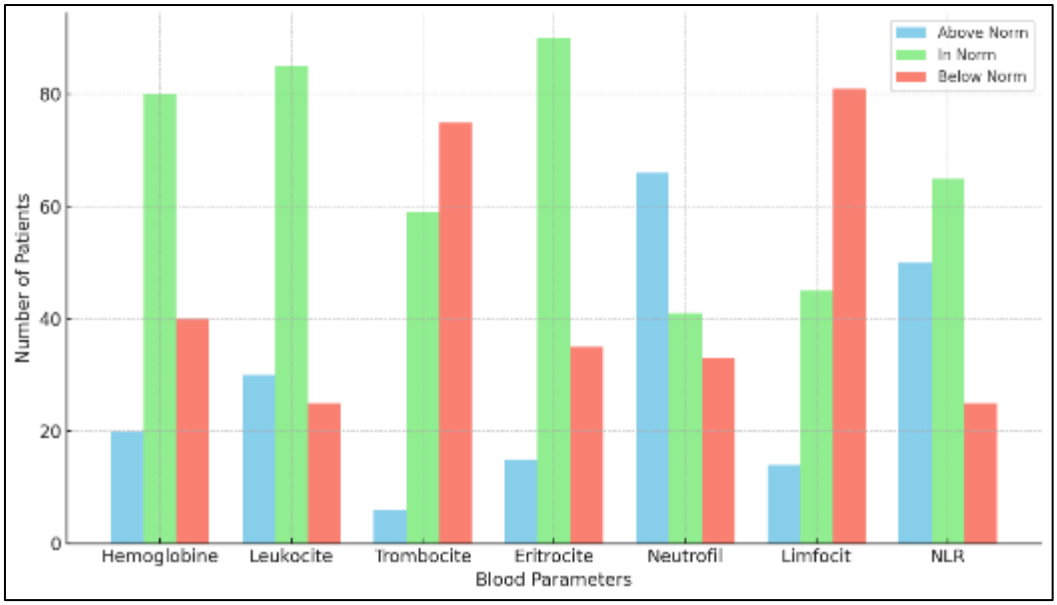

Figure 2 Complete Blood Count Parameters in patients of the study

3.1. Neutrophils

47.1% of patients showed elevated neutrophil levels, a common response in infections, indicating that many patients experienced increased immune activity. However, 23.6% had neutrophil counts below normal, suggesting immune suppression or a reduced immune response in some cases.

3.2. Lymphocytes

The data show that 57.9% of patients had lymphocyte levels below normal, a finding often associated with viral infections, including COVID-19. A smaller portion (10%) showed elevated lymphocyte levels, possibly reflecting a recovery phase or co-existing infections.

3.3. Platelets

Interestingly, a high percentage (53.6%) of patients had low platelet counts (thrombocytopenia), which can occur due to inflammation, viral replication, or other COVID-19-related factors. Only a small percentage (4.3%) showed elevated platelet counts.

3.4. Hemoglobin and Red Blood Cells

The majority of patients had normal hemoglobin (57.1%) and red blood cell (RBC) levels (64.3%). However, a notable percentage had abnormal values 28.6% and 25%, respectively indicating reduced levels, possibly linked to anemia or inflammation.

3.5. Leukocytes

Most patients had normal leukocyte levels (60.7%), although 21.4% showed elevated values, reflecting active infection, while 17.9% had decreased levels, suggesting possible immune suppres1sion.

3.6. NLR (Neutrophil-to-Lymphocyte Ratio)

An elevated NLR was found in 35.7% of patients, which is typically associated with inflammation and poorer outcomes in infections such as COVID-19.

Table 5 Correlation between Length of Hospital Stay and Neutrophil Levels

	1-5 Days	>5 Days	Total
Normal range of neutrophils	20	21	41
Neutrophilia	34	32	66
Neutropenia	10	23	33
Total	64	76	140

In this table, we can see that 32 out of 66 patients with elevated neutrophil levels had longer hospital stays (>5 days), while 34 stayed for 1–5 days. For patients with normal neutrophil levels, the distribution is fairly balanced (20 stayed for 1–5 days and 21 stayed >5 days).Patients with lower neutrophil counts mostly stayed for more than 5 days (23 out of 33).

Table 6 Correlation between Lymphocyte Levels and Presence of Respiratory Symptoms

	Presence of respiratory symptoms	Without respiratory symptoms	Total
Normal Lymphocytes	25	20	45
Lymphopenia	69	12	81
Lymphocytosis	8	6	14
Total	102	38	140

Among 81 patients with lymphocyte levels below normal, 69 had respiratory symptoms, suggesting a strong association between lymphopenia and respiratory complications. In contrast, patients with normal lymphocyte counts had a more balanced distribution between those with (25 patients) and without (20 patients) respiratory symptoms.

Tabel 7 Correlation between CRP Levels and Platelets

	PCR normal	High PCR normë	Total
Normal Platelets	37	22	59
Thrombocytopenia	26	49	75
Thrombocytosis	0	6	6
Total	63	77	140

49 out of 75 patients with low platelet counts had elevated CRP levels, whereas those with normal platelet counts had more patients with normal CRP levels (37 out of 59). Thrombocytopenia is associated with higher inflammation (as indicated by increased CRP) in these patients.

4. Discussions

The results of this study highlight the profound impact that COVID-19 has on hematologic parameters, affecting both the severity of symptoms and the recovery trajectory. According to our study, the dominant age group was under 12 months old, accounting for 31.4%, followed by the 4–10 years age group with 30.7%, and the least affected was the 1–3 years group with 18.6%. This aligns with data from the literature, mainly from European countries such as Italy and England. (12,19) Meanwhile, studies from the American continent showed that the most affected age group was 13–17 years old. Males were more affected than females, representing 60% of cases, consistent with data from all reviewed studies.

The majority of patients stayed hospitalized for more than a week, specifically 47.9% of them. Among comorbidities, respiratory tract diseases dominated with 7.1% of cases, followed by Type 1 Diabetes Mellitus in 5.7% of cases, and lastly urinary tract pathologies with 2.9%. Descriptive analysis of hematologic and inflammatory parameters showed

important trends across the study population. Among 140 pediatric patients, 67.1% had respiratory symptoms, 18.6% had gastrointestinal symptoms, and 14.3% had other symptoms.

47.1% of patients had elevated neutrophil levels. Elevated neutrophil levels consistently appeared as key indicators of severe outcomes, including longer hospital stays and development of respiratory complications. This corresponds with existing literature showing neutrophilia as a marker of inflammation and tissue damage, commonly seen in severe COVID-19 cases. Chi-square tests revealed significant associations between hematologic markers and clinical outcomes. Elevated neutrophil levels were significantly associated with longer hospital stays, with 32 out of 66 patients staying more than 5 days ($p < 0.05$).

The study showed that 57.9% of patients had decreased lymphocyte levels. Lymphopenia, another important finding in this study, was strongly associated with more severe clinical conditions. Decreased lymphocytes are commonly seen in viral infections, including COVID-19, and reflect immune suppression, which may contribute to the persistence of symptoms such as respiratory distress. Similarly, low lymphocyte levels were strongly associated with the presence of respiratory symptoms, as 69 out of 81 patients with low lymphocytes exhibited respiratory symptoms ($p < 0.05$).

Thrombocytopenia was observed in 53.6% of patients. Interestingly, platelet levels showed a tendency towards being protective, although not statistically significant. This may suggest that thrombocytopenia in pediatric COVID-19 patients is not as strongly associated with respiratory symptoms as in adults, although further research is needed.

5. Conclusion

This study demonstrates that hematologic markers, particularly neutrophil, lymphocyte, and platelets levels, are key predictors of clinical outcomes in pediatric post-COVID-19 patients. These markers play an essential role in determining the severity of respiratory symptoms and the length of hospital stay. Monitoring these parameters can guide clinical management, improving patient care and outcomes.

Recommendations

It is recommended to routinely monitor key hematologic in pediatric COVID-19 patients to assess disease severity and predict clinical outcomes. Early screening for elevated neutrophil levels should be implemented to identify high-risk patients and initiate timely interventions. Additionally, close monitoring of lymphocyte levels is essential to prevent complications related to immune suppression and coagulation abnormalities.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

"Ethical approval to report this research article was obtained from General Pediatric Ward.

Statement of informed consent

Informed Consent was taken from the parents of the hospitalized child, reported in the study, for using the data of the medical records, providing anonymity.

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